REMARKS

In view of the above amendments and the following remarks, reconsideration and allowance of this application are requested. Claims 1, 5-10, 18, 29, 35, 37 are pending, with claims 1 and 29 being independent. Claims 1, 5, 10, and 29 are currently amended and support for the amendments may be found, for example, in the application as filed at Page 4, Lines 16-21.

In the Office Action dated August 7, 2009, the Examiner rejected claim 18 under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner seeks clarity on the term "one or more non-functional layers surrounding the tablet."

Applicants hereby submit that the term "one or more non-functional layers surrounding the tablet" has been described in the specification on Page 5, lines 14-16 and Lines 31-32 as being a cosmetic coating which does not have any role in altering the release of the active ingredient present in the other layer. This optional non-functional layer is solely for cosmetic purposes and does not affect the release of alfuzosin (which is the function of the dosage form).

In the Office Action dated August 7, 2009, the Examiner rejected claims 1, 5-9 and 18 under 35 U.S.C. § 102(b) as being anticipated by Ayer et al. (U.S. 6,096,339). Ayer discloses "a composition comprising the active ingredient verapamil hydrochloride, hydroxypropyl methylcellulose ("**HPMC**") and hydroxypropyl cellulose ("**HPC**"). Further, the dosage form manufactured by this procedure comprises a drug composition, a push displacement composition, a subcoat and an outer wall. *See* Col. 6, Line 17-36. The dosage forms are primarily related to a "push-displacement composition in contacting layered arrangement compris[ing] a polymer that imbibes an aqueous or

biological fluid and swells to push the drug composition through the exit means from the dosage form. *See* Col. 15, Lines 16-19. Ayer also discloses that the binder polypvinylpyrrolidone and the lubricant magnesium stearate may be present in the dosage form. *See* Col. 6, Lines 21-23. Finally, alfuzosin can be delivered by the dosage form. *See* Claim 16.

The dosage forms disclosed and exemplified in Ayers are osmotic dosage forms, i.e., they typically are, at a minimum, a bi-layered dosage form, which comprises a drug composition layer that includes a hydrophilic polymer in combination with a push composition layer for displacing the drug composition from the dosage form. The push composition layer imbibes fluid and expands and displaces the drug composition layer from the dosage form. The drug is delivered at a substantially uniform and non-varying rate of release over time.

In osmotic dosage forms, osmotic pressure is the driving force that generates a constant drug release. The system is fabricated by applying a semi-permeable membrane around a core of an osmotically active drug or over a core of an osmotically inactive drug in combination with an osmotically active salt.

Applicants' present invention seeks to develop a matrix type formulation. These formulations do not use osmotic forces to effectuate drug release, but instead rely on diffusion or erosion of the tablet matrix itself to control the release. The present matrix formulation is formulated with a single functional layer, whereby release retarding polymers are mixed with the active ingredient to form a solid dosage form. In the present application, both HPMC and HPC are combined to form the release retarding agent.

Applicants' presently amended claim 1, requires that the dosage form be formulated such that there is only one functional layer. This single functional layer is composed of the active ingredient, alfuzosin, and the release retarding agent, HPMC and

HPC. The produced dosage form functions as a matrix type formulation and does not use any osmotic forces to sustain drug release.

Ayers does not disclose a dosage form composed of a single functional layer, where the functional layer includes alfuzosin, HPMC and HPC. As such, claim 1 is allowable over Ayers. Claims 5-9 and 18 depend from claim 1 and are allowable over Ayers for the same reason that claim 1 is allowable over Ayers.

The Examiner also rejected claims 1, 5-9 and 18 under 35 U.S.C. § 103(a) as being unpatentable over Ayer et al. (U.S. 6,096,339). As discussed above, Ayers is directed to a sustained release formulation designed to utilized osmotic forces in order to deliver the active ingredient over a prolonged period of time. Ayers does not disclose, or motivate a person skilled in the art to try, matrix formulations. There is no disclosure or teaching of a dosage form that includes a single functional layer, whereby a sustained release profile is obtained through simple erosion or diffusion of release retarding agents, namely HPMC or HPC.

A person skilled in the art would not be motivated by Ayers to modify the bi-layered osmotic dosage form disclosed into a single layer matrix formulation. These two dosage forms, osmotic and matrix, are fundamentally different formulations, operating in two separate and distinct manners. As such, claim 1 is allowable over Ayers. Claims 5-9 and 18 depend from claim 1 and are allowable over Ayers for the same reason that claim 1 is allowable over Ayers.

The Examiner has also rejected claims 1, 5-10 and 18 under 35 U.S.C. § 103(a) as being unpatentable over Maggi et al. (U.S. 6,149,940). Maggi discloses two or three layer tablets wherein layer 2 contains alfuzosin hydrochloride with hydrophilic polymers and a first layer and optional third layer containing hydrophilic polymers. Maggi discloses a "pharmaceutical tablet containing two or three layers, characterized in that it

has the following structure: (a) a first layer 1 having the property of swelling considerably and quickly on contact with aqueous biological fluids...and (b) a second layer 2 adjacent to the first layer, in which the alfuzosin hydrochloride is conveyed. *See* Col. 2, Lines 4-19. "The invention is characterized in that on contact with gastric juices, after rapid and considerable swelling of at least one of the layers...the pharmaceutical preparation increases considerably in volume; thus, the pharmaceutical preparation remains in the stomach for longer. In this way, most of the alfuzosin hydrochloride contained may be absorbed in a controlled manner in that portion of the gastrointestinal tract which has the highest capacity for absorption." *See* Col 2, Lines 27-36.

Maggi teaches away from the use of "preparations such as hydrophilic matrices, which break down or swell." *See* Col. 1, Lines 42-44. Maggi states that these types of formulations "have major drawbacks in the cases [of] where active substances per se would be conveyed, such as alfuzosin, having a more intense absorption at the duodenum-jejunum level which decreases thereafter in the tract. Indeed, in this case, only a very limited amount of the active substance conveyed maybe absorbed and thus exert the desired therapeutic activity, whereas most of the medicinal product released by the pharmaceutical preparation cannot be absorbed since, in lower portions of the gastrointestinal tract, the biological barriers are relatively incapable of allowing the medicinal product to pass." *See* Col. 1, Lines 56-67.

The present invention is a sustained release tablet comprising a single functional layer, which comprises alfuzosin and a release retarding agent, whereby the release retarding agent is a composed of both HPMC and HPC. This formulation may generally be deemed a hydrophilic matrix preparation, and thus one skilled in the art would not be motivated by Maggi to modify the disclosure therein in such a way as to reach the present invention. Such a modification would be against the teachings in Maggi and be contrary to the overall purpose of the invention. Furthermore, there is no teaching or motivation

in Maggi to reduce the number of functional layers down to a single layer in order to simplify the manufacturing process.

As such, claim 1 is allowable over Maggi et al. Claims 5-10 and 18 depend from claim 1 and are allowable over Maggi for the same reasons that claim 1 is allowable over Maggi.

The Examiner has also rejected claims 1, 5-10 under 35 U.S.C. § 103(a) as being unpatentable over Maggi et al. (U.S. 6,149,940) in light of Remington The Science and Practice of Pharmacy, page 894 (2000). As discussed above, Maggi teaches away from the hydrophilic matrix formulation of the present invention. Remington, in general, teaches that there are many reasons to add coatings to tablets that are already functionally complete. Remington discloses a brief history of the evolution of the coating process, and how film coating came to be.

However, Remington fails to cure the deficiencies in Maggi, namely, Remington does not discuss the advantages of using a hydrophilic matrix formulation composed of a single functional layer, which includes a release retarding agent, and would not motivate one skilled in the art to formulate an alfusozin dosage form in such a manner. Therefore, for the same reasons that claim 1 is allowable over Maggi et al, claim 1 is also allowable of Maggi in light of Remington. Claims 5-10, 18 depend from claim 1 and are allowable over Maggi in light of Remington for the same reasons that claim 1 is allowable over Maggi in light of Remington.

The Examiner has also rejected claims 1, 5-10 under 35 U.S.C. § 103(a) as being unpatentable over Bordes et al. (U.S. 2004/0115259). Bordes discloses a pharmaceutical dosage form of alfuzosin, whereby such dosage form is formulated as a floating tablet. Bordes states that "it will be seen that the proportion of excipient is very important relative to that of the active principle. It was not obvious that such a ratio could lead to

immediate flotation and that it cold lead to control of the release profiles as has been indicated above." See Paragraph [0082].

By Bordes own disclosure, substitution and alteration of the excipients used in the formulations is not obvious, and any alterations may affect the precise ratio of excipient to active ingredient; such a ratio is a critical feature in preparing a dosage form that floats. In addition, there is no teaching that both HPMC and HPC may be used in combination in a single functional layer. Any modifications to the examples in Bordes may affect the underlying goal of the inventions, namely, that the product floats in the stomach.

A person skilled in the art would heed such a warning, and would not be motivated to substitute and/or add HPC to the functional layer. In addition, the combination of HPMC and HPC may effect the compression necessary to enable that the dosage form floats in the stomach.

Not without extensive trial and error would someone skilled in the art be able to modify the disclosure in Bordes to come up with the present invention. As such, claim 1 is allowable over Bordes et al. Claims 5-10 depend from claim 1 and are allowable over Bordes for the same reasons that claim 1 is allowable over Bordes.

The Examiner has also rejected claims 1, 5-10 under 35 U.S.C. § 103(a) as being unpatentable over Bordes et al. (U.S. 2004/0115259) in light of Lowey (U.S. 4,259,314). For the reasons discussed above, Bordes would not motivate one skilled in the art to modify its disclosure to come to the present invention.

Further, the additional teachings of Lowey do not cure those deficiencies. Even if a person skilled in the art would be directed to read Lowey in the first place (it does not disclose alfuzosin), the ratio of excipient to active ingredient that is deemed critical by

Bordes would not be addressed; these ratios vary according to the nature of the active ingredient and alfuzosin is not addressed. Therefore, a person skilled in the art would not know how to modify Bordes in light of Lowey to reach the present invention. Only with hindsight or extensive experimention is it possible to determine the proper ratio of HPMC and HPC in combination with alfuzosin in a single functional layer.

Therefore, claim 1 is allowable over Bordes et al in light of Lowey. Claims 5-10 depend from claim 1 and are allowable over Bordes and Lowey for the same reasons that claim 1 is allowable over Bordes and Lowey.

The Examiner has also rejected claims 1, 5-10 and 18 under 35 U.S.C. § 103(a) as being unpatentable over Bordes et al. (U.S. 2004/0115259) in light of Remington The Science and Practice of Pharmacy, page 894 (2000). For the reasons discussed above, Bordes would not motivate one skilled in the art to modify its disclosure to come to the present invention.

Further, Remington does not cure those deficiencies, as it provides no motivation, except to add an additional coating to the single functional layer. However it does not motivate one skilled in the art to alter the excipient ratio through the inclusion of both HPMC and HPC in the functional layer.

As such, claim 1 is allowable over Bordes et al in light of Remington. Claims 5-10, 18 depend from claim 1 and are allowable over Bordes and Remington for the same reasons that claim 1 is allowable over Bordes and Remington.

Conclusion

For the reasons stated above, the Examiner is urged to pass claims 1, 5-10, 18, 29, 35, and 37 to issue.

Respectfully submitted,

James J. DeYonker
Reg. No. 52,817

Date: November 09, 2009

Ranbaxy Laboratories Limited
600 College Road East, Suite 2100
Princeton, New Jersey 08540
Tel: (609) 720-5394
Fax: (609) 514-9779